#40 DMT 8-1-03

PATENT APPLICATION

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application

Brockhaus et al.

Group: 1646

Serial No. 08/444,790, filed May 19, 1995

Examiner: J. Murphy

For: **HUMAN TNF RECEPTOR**

COMMUNICATION

Nutley, New Jersey 07110
January 21, 2003

Commissioner of Patents
Washington, D.C. 20231

Dear Sir:

This Communication is filed in response to the August 21, 2002 Office Action issued in connection with the above-identified patent application. A response to this Office Action was originally due November 21, 2002. A two-month extension of time is being requested concurrently. Accordingly, a response to the Office Action is now due January 21, 2003.

Reconsideration is requested in view of the following remarks. Claims 55 and 62-99 are pending in the subject application. Claim 55 has been withdrawn from consideration by the Patent Office. Claims 78-99 were added in a Supplemental Amendment dated August 7, 2002 (a copy of this Supplemental Amendment is submitted herewith). Claims 78-99 were not addressed in the Office Action. However, consideration of these claims is earnestly solicited. As pointed out in the Supplemental

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Amendment dated August 7, 2002, U.S. Patent No. 6,271,346 (submitted to the Patent Office as Document A10) also claims DNA that encodes the p55 TNF receptor.

Applicants thank the Patent Office for providing selected Forms PTO-1449 that were initialed by the Examiner as having been considered. However, still outstanding are the Forms PTO-1449 that were filed with the Communication and Information Disclosure Statement dated October 17, 2001, the Supplemental Information Disclosure Statement dated January 7, 2002, and the Supplemental Information Disclosure Statement dated July 26, 2002. Consideration of all submitted documents is requested, as is the return of initialed Forms PTO-1449 indicating that they have been considered. To avoid a future issue, note that certain document numbers on the numerous Forms PTO-1449 identify more than one document. Accordingly, the file should be reviewed by the Patent Office prior to issuance to ensure that all documents are properly listed on the face of the patent when issued.

Claims 62-77 were again rejected under 35 U.S.C. §102(e) as allegedly being anticipated by Wallach I (U.S. Patent No. 5,981,701).[1] The Office Action stated:

> Applicant argues that the TNF inhibitory protein disclosed by Wallach is a different protein that can be isolated from human urine (Paper No. 34 at 2) and that the amino acid sequence of the Wallach protein is different from the protein claimed in the instant application in that they have different amino terminal sequences (Paper No. 34 at 3). However, the full amino acid sequence of the TNF inhibitory protein of Wallach is set forth in the '261 patent (see SEQ ID NO. 2). The sequence of SEQ ID NO. 2 of the '261 patent is 100% identical from amino acids 1-180 of the protein claimed

[1] Applicants point out that rejections based on analogous Wallach documents have been overcome in related applications and that claims 62-77 were previously found to be allowable by the Patent Office (see, for example, Paper 32).

in the instant application. Thus, claims 62-66, 69, 72, 75 are anticipated. The methods to produce the TNF inhibitor protein from host cells are disclosed in the Wallach patent (column 12, line 11-column 15, line 53), thus anticipating claims 67-68, 70-71, 73-74, 76-77.

The Patent Office also rejected claims 62-77 for allegedly being anticipated by U.S. Patent No. 5,811,261 ("Wallach II").

Contrary to the position set forth in the Office Action, Wallach I does not disclose applicants' claimed invention. In addition, anticipation under 35 U.S.C. § 102 requires all limitations of the claimed invention must be found within the "four corners" of a single document. In the present rejection, the Patent Office has taken the disclosure of Wallach I and combined it with the disclosure of Wallach II. In essence, the Patent Office's position is that Wallach I did not mean to disclose the wrong sequence but rather meant to disclose the later identified sequence found in Wallach II. As will be detailed below, Wallach II is not prior art with respect to SEQ ID NO. 2 and therefore cannot serve as a basis for rejection.

Applicants' Claimed Invention

Applicants' claimed invention relates to homogenous protein that binds human tumor necrosis factor. Independent claim 62 requires that the protein have an apparent molecular weight of about 55 kilodaltons on a non-reducing SDS-polyacrylamide gel and comprises the amino acid sequence of Figure 1. Independent claim 63 requires that the protein comprises the amino acid sequence of Figure 1 beginning at amino acid number 1 and ending approximately at amino acid number 180. Independent claim 66 requires that the protein has an apparent molecular weight of about 55 kilodaltons on a non-reducing SDS-polyacrylamide gel and is encoded by the DNA sequence of Figure 1. Independent

claim 69 requires that the protein comprises the amino acid sequence encoded by the DNA sequence of Figure 1 beginning at nucleotide number 121 and ending at approximately nucleotide number 627.

Wallach I

Wallach I discloses a different TNF inhibitory protein that can be isolated from human urine. While Wallach I generally discloses recombinant techniques together with the suggestion to try such techniques on the Wallach I TNF inhibitory protein, there is no disclosure of any recombinantly produced TNF inhibitory protein.

Amino Acid Sequence

The amino acid sequence of Wallach I is different from the amino acid sequence of applicants' claimed proteins. The protein of Wallach is characterized by containing at its N-terminus the following amino-acid sequence: Asp-Ser-Val-Cys-Pro-Gln-Gly-Lys-Tyr-Ile-His-Pro-Gln-X-Asn-Ser (Wallach, column 4, lines 26-39, column 10, lines 21-28, and column 12, lines 12-23). In marked contrast, applicants' claimed amino acid sequence of Figure 1 beginning at amino acid number 1 is: Leu-Val-Pro-His-Leu-Gly-Asp-Arg-Glu-Lys-Arg-Asp-Ser-Val-Cys-Pro. Since the protein of Wallach and applicants' claimed receptor protein have different N-terminus amino acid sequences, they are clearly different proteins, and thus patentably distinct from each other.

Applicants' claims 62-68 recite the above-mentioned N-terminus amino acids. Accordingly, the invention of these claims is neither taught nor suggested in Wallach I.

Applicants' amino acid sequence encoded by the DNA sequence of Figure 1 beginning at nucleotide number 121 and ending at approximately nucleotide number 627

is not disclosed in Wallach I. Claims 69 and dependent claims 70-77 are directed to a homogeneous protein that comprises the amino acid sequence encoded by the DNA sequence of Figure 1 beginning at nucleotide number 121 and ending at approximately nucleotide number 627. As stated above, Wallach I does not teach or suggest applicants' claimed homogeneous receptor protein (claims 62 and 66). Although Wallach I discloses the possibility that its protein may contain "active fractions" (Wallach at column 4-5 bridging paragraph), Wallach I provides no guidance for selecting any particular fraction. Since Wallach fails to provide any guidance with respect to identifying particular active fragments of its own protein, Wallach I clearly cannot provided guidance for identifying active fragments in a different protein. Accordingly, no teaching or suggestion in Wallach I could render obvious applicants' amino acid sequence encoded by the DNA sequence of Figure 1 beginning at nucleotide number 121 and ending at approximately nucleotide number 627.

Applicants' claims 70-77 contain the above-mentioned amino acid sequence that is nowhere found in Wallach I. Accordingly, these claims are neither taught nor suggested by Wallach I.

Molecular Weight

Contrary to the Patent Office's position of record, Wallach I does not disclose a protein that "has a molecular weight of 40-80 kD." Wallach I discloses that when "crude preparations thereof derived from human urine concentrate were chromatographed under Ultrogel ACA 44 gel filtration column, it [sic.] showed an apparent molecular weight of 40-80 Kda" (Wallach, column 4, lines 12-16). This molecular weight was for a **crude preparation**, not a homogenous protein as in applicants' claimed invention. Wallach I states that the "substantially purified protein, which is substantially free of proteinacous

impurities, has a molecular weight of about 26-28 Kda when analysed by SDS.PAGE under reducing conditions" (Wallach I, column 4, lines 16-21). In distinction, applicants' claims 62 and 66-68 recite an apparent molecular weight of about 55 kilodaltons on a non-reducing SDS-polyacrylamide gel. The Wallach I protein has a molecular weight that differs from that claimed by applicants.

With respect to 35 U.S.C. § 102, the disclosure of Wallach II is irrelevant. Anticipation based on 35 U.S.C. § 102 must be found in a single document. Moreover, for the reasons discussed below, the disclosure of Wallach II relied on by the Patent Office is not prior art.

Applicants' claimed proteins differ in both amino acid composition (in particular at the N-terminus) and molecular weight, in claims where molecular weight is recited, from those disclosed in Wallach I.

Wallach II

The disclosure of Wallach II that forms the backbone of the Patent Office's rejection under 35 U.S.C. § 102 is not prior art. Wallach I and Wallach II share a common progenitor, specifically, U.S. Application No. 07/243,092, filed September 12, 1988. Whereas Wallach I contains text is similar to that of the progenitor application, Wallach II contains substantial new material that was added in Application No. 07/625,668, filed December 13, 1990. This new material includes SEQ ID NO. 2 upon which the Patent Office's rejection is based. The effective date of Wallach II as prior art under 35 U.S.C. § 102(e) with respect to this new material is December 13, 1990. Applicants are entitled to the benefit of their September 10, 1990 filing date under 35 U.S.C. § 120 (applicants may also rely upon earlier dates under 35 U.S.C. § 119). Since applicants' effective date

antedates the effective date of Wallach II as prior art under 35 U.S.C. § 102(e), Wallach II cannot form a basis for rejection under 35 U.S.C. §§ 102 or 103.

In view of the above, applicants request reconsideration, withdrawal of all rejections under 35 U.S.C. §102, and the issuance of a Notice of Allowance.

If a telephone conference would be of assistance in furthering prosecution of the subject application, applicants request that the undersigned attorney be contacted at the number below.

No fee, other than the fee for a two-month extension of time, is required in connection with the filing of this Communication. If any additional fees are deemed necessary, authorization is given to charge the amount of any such fee to Deposit Account No. 08-2525.

Respectfully submitted,

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